optical density changes resulting from hydrolysis of the substrate or other assay reagents.

3. (amended) A method of diagnosing acute pancreatitis in a patient suspected of suffering from acute pancreatitis comprising:

(a) measuring carboxypeptidase A levels in a biological fluid from a patient by detecting changes in optical density resulting from hydrolysis of a carboxypeptidase A substrate by any carboxypeptidase A in the biological fluid in the presence and absence of a carboxypeptidase A specific inhibitor, wherein the presence of the carboxypeptidase A specific inhibitor corrects for any extraneous optical density changes resulting from hydrolysis of the substrate or other assay reagents; and

(b) determining whether the measured levels of carboxypeptidase A in the biological fluid of the patient corrected for any extraneous optical density changes resulting from hydrolysis of the substrate or other assay reagents are elevated over levels in biological fluid from a healthy control population.

REMARKS

At the outset, Applicant thanks Examiner Leary for the time and consideration in conducting multiple telephone interviews relating to this case.

Claims 1-5 are pending in the instant application. The Examiner has acknowledged claims 4 and 5 to be allowable. However, the Examiner has maintained the rejections of claims 1-3 as being anticipated by Sugiyami et al. (U.S. Patent No. 4,551,272) or Sugiyami et al. (U.S. Patent 4,432,896) or rendered obvious over Brown et al. (1987) in combination with Talley (1990).

As discussed in detail with the Examiner during the Interview on January 25, 2001, while the Sugiyami patents suggest that their assay is measuring carboxypeptidase, it was later discovered that this assay was actually measuring the proenzyme. The fact that assays such as that taught by Sugiyami were measuring the proenzyme and not carboxypeptidase A is clearly supported by references by Stewart and Gilvarg (Clinical Chimica Acta 1999 281:19-28; Clinica Chimica 2000 292:107-115), copies of which were provided to the Examiner for review after the January 25, 2001 Interview. Accordingly, the cited prior art patents do not actually teach a method of measuring carboxypeptidase A levels as claimed in claims 2 and 3 of the instant application.

Further, Applicant has amended claims 1, 2 and 3 to specify that the measured carboxypeptidase levels are compared to any activity measured in a blank containing the sample and a specific inhibitor of the enzymatic activity to correct for extraneous

changes in measurement unrelated to enzymatic activity of the sample. Support for this amendment can be found in the specification at page 7, line 31 through page 8, line 19.

None of the prior art references teach or suggest a method with this step.

The Examiner suggests that the reaction termination solution of the Sugiyami patents meets the limitations of a specific inhibitor. Applicant respectfully disagrees. However, even if this were true, the Sugiyami patents do not teach comparing the measured enzymatic activity to any activity measured in a blank containing the sample and a specific inhibitor of the enzymatic activity to correct for extraneous changes in measurement unrelated to enzymatic activity of the sample. Since this step of the assay is not taught in the Sugiyami patents, the patents cannot anticipate the claims as amended.

The combination of Brown et al. and Talley et al. also fail to teach to or suggest this limitation of amended claims 1, 2 and 3.

As acknowledged by the Examiner in the Office Action mailed November 22, 2000, Brown does not state that a specific inhibitor can be present in a method step for measuring enzymatic activity in a sample. Nor does Brown teach or suggest the step of comparing the measured enzymatic activity to any activity measured in a blank

containing the sample and a specific inhibitor of the enzymatic activity to correct for extraneous changes in measurement unrelated to enzymatic activity of the sample.

Talley et al. (1990) teach a method of preparing (R)-succinic acid derivatives and state that the activity of carboxypeptidase A is inhibited by one of these derivatives. No assay whatsoever for carboxypeptidase A is taught in this reference. Accordingly, this reference also fails to teach or suggest the step of comparing the measured enzymatic activity to any activity measured in a blank containing the sample and a specific inhibitor of the enzymatic activity to correct for extraneous changes in measurement unrelated to enzymatic activity of the sample.

Thus, the combination of Brown et al. and Talley et al. fails to teach or suggest all the limitations as set forth in the claims as amended, and therefore does not establish a *prima facie* case of obviousness.

Withdrawal of the rejections of claims 1-3 under 35 U.S.C. § 102 and 103 and allowance of pending claims 1-5 of the instant application is therefore respectfully requested.

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

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LICATA & TYRRELL P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515